

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau

INTERNATIONAL BUREAU OF PATENT COOPERATION  
3, rue de la Harpe, 1205 Yverdon, Switzerland  
Tel. (41) 26 30 65 11, Fax (41) 26 30 65 12  
E-mail: info@wipo.int, PCT@wipo.int

(43) International Publication Date  
10 August 2000 (10.08.2000)

PCT

(10) International Publication Number  
WO 00/46187 A3

(51) International Patent Classification: C07C 211/01, A61K 31/132

(74) Agents: LAU, Kawai et al.; Morrison &amp; Foerster LLP, 2000 Pennsylvania Avenue, N.W., Washington, DC 20006-1888 (US).

(21) International Application Number: PCT/US00/02972

(22) International Filing Date: 4 February 2000 (04.02.2000)

(81) Designated States (national): AL, AM, AU, AZ, BA, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN.

(25) Filing Language: English

(26) Publication Language: English

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(30) Priority Data: 60/118,892 5 February 1999 (05.02.1999) US

(71) Applicant: ORIDIGM CORPORATION [US/US]; Suite 200, 4010 Stone Way North, Seattle, WA 98103 (US).

Published:  
— With international search report.

(71) Applicants and

(72) Inventors: VERMEULIN, Nicolaas, M., J. [US/US]; 19334 - 196th Avenue NE, Woodinville, WA 98072 (US). BURNS, Mark, R. [US/US]; 226 Northwest 184th Street, Shoreline, WA 98177 (US). WEBB, Heather, K. [US/US]; 5705 Seaview Avenue, NW, Seattle, WA 98107 (US).

(88) Date of publication of the international search report: 14 December 2000

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 00/46187 A3

(54) Title: ANTIZYME MODULATORS AND THEIR USE

(57) Abstract: The present invention is directed to agmatine and polyamine analogs and their use as drugs, as well as agricultural or environmentally useful agents. As drugs, the analogs decrease cellular polyamine levels, possibly by inducing antizyme, and can be used to treat disorders of undesired cell proliferation, including cancer, viral infections and bacterial infections. The analogs may be utilized in pharmaceutical compositions either alone or in combination with other agents, particularly other inhibitors of polyamine synthesis or transport, but including other inhibitors of cell proliferation. The analogs are not necessarily metabolized to contribute to the polyamine pool and are designed to enter cells by pathways independent of polyamine transport. The invention further defines structural elements/motifs within these analogs that are key to their induction of antizyme.

## INTERNATIONAL SEARCH REPORT

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07C211/01 A61K31/132		International Application No PCT/US 00/02972
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07C A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 03823 A (O DAY CHRISTINE L ; BURNS MARK R (US); ORIDIGM CORP (US); WEBB HEAT) 28 January 1999 (1999-01-28) cited in the application figure 2	1-10,25
X	US 5 498 522 A (PORTER CARL W) 12 March 1996 (1996-03-12) claims 1-35	1-17,25
X	US 5 677 350 A (FRYDMAN BENJAMIN J) 14 October 1997 (1997-10-14) claims 1-18	19-22,25
-/-		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "S" documents member of the same patent family		
Date of the actual completion of the international search 12 July 2000		Date of mailing of the international search report 07.08.00
Name and mailing address of the ISA European Patent Office, P.B. 5016 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Goetz, G

Form PCT/ISA/210 (second sheet) (July 1992)

page 1 of 2

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/02972

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 129, no. 12, 21 September 1998 (1998-09-21) Columbus, Ohio, US; abstract no. 147272, SATRIANO, JOSEPH ET AL: "Agmatine suppresses proliferation by frameshift induction of antizyme and attenuation of cellular polyamine levels" XP002142375 abstract & J. BIOL. CHEM. (1998), 273(25), 15313-15316 ,	1-27
X	BEILSTEIN INFORMATION SERVICE FILE: XFIRE, XP002142374 see BRN: 1719247, 1735364, 1732596, 1735401	19-23

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/02972**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 26 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-27 partially  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210.
3. ☐ Claims Nos.:  
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1999)

International Application No. PCT/US 00 02972

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.2

Claims Nos.: 1-27 partially

1. The wording "wherein said analog induces expression of full-length antizyme" renders the scope of present claims 1 to 24 unclear. Such an intended definition for a compound is to be regarded as a mere result to be achieved and not as a feature characterizing a compound. Due to this definition it is not clear neither from the claims nor from the description, if the application is directed to the compounds per se or to the use of the compounds for induction of expression of full-length antizyme.

It is further noticed that such a use (induction of expression of full-length antizyme) in itself is no clear medical use.

2. Present claims 1-9, 11-17, 19-22 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. In particular due to the unclear definition "analog" as well as to the unlimited definitions of the possible groups and substituents ("substituted alkyl, alkenyl, multi-ring substituted aliphatic" etc. a meaningful search is impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/02972

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9903823 A	28-01-1999	AU 8496898 A EP 1001927 A	10-02-1999 24-05-2000
US 5498522 A	12-03-1996	CA 2094341 A EP 0568338 A JP 6062896 A	29-10-1993 03-11-1993 08-03-1994
US 5677350 A	14-10-1997	AU 6381996 A WO 9640096 A	30-12-1996 19-12-1996